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EXAMINER	
CARLSON, KAREN C	
ART UNIT	PAPER NUMBER
1656	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/763,502	ST. GEORGE-HYSLOP ET AL.	
	Examiner	Art Unit	
	Karen Cochrane Carlson, Ph.D.	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 August 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *34-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/5/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

This Office Action is in response to the paper filed August 15, 2007.

Claims 1-33 have been cancelled. Claims 34-37 are currently pending and are under examination.

Benefit of priority is to April 1, 1999.

Withdrawal of Objections and Rejections:

The objection to the disclosure is withdrawn.

Maintenance of Rejections, modified due to amendment

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 34-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In Claim 34, again, there is no function assigned to the "function conservative fragment" of PAMP.

In Claim 36, again, it is not clear what the biochemical changes similar to muations in PS-1, PS2, or beta- amyloid are.

In Claim 35, a mutant PAMP that is substantially homologous to human, mouse, or D. melanogaster PAMP is not clear. That is, are man-made mutations in human, mouse, or D. melanogaster PAMP considered substantially homologous, or are other species of PAMP considered mutant PAMPS? The term "substantially homologous" is indefinite, that is, what regions are homologous and which are not?

Applicants urge that several potential functions of PSMP based on sequence motifs are set forth in the specification at pages 7-9 and therefore one skilled in the art would understand the term function-conservative fragment of PAMP. The intended function of the fragment is not set forth in the claim. In order for one skilled in the art to determine which fragment of PAMP is intended, an assayable function must be attributed to the fragment. Thus, the argument is not persuasive.

Applicants argue that biochemical changes similar to mutations in PS2, PS2, and beta amyloid are clear and cite beta catenin tralocation a secretase mediated beta APP processing as examples. Again, the intended function of the mutant PAMP is not set forth in the claim. In order for one skilled in the art to determine which mutant PAMP is intended, an assayable function must be attributed to the mutant. Thus, the argument is not persuasive.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 35 and 36 are rejected under 35 U.S.C. 102(a) as being anticipated by The C. *elegans* Sequencing Consortium (December 11, 1998; Science 282:2012-2018; see the sequence alignment for SEQ ID NO: 12 attached to the previous office action).

The Consortium teaches an amino acid sequence that shares 99.7% identity to SEQ ID NO: 12 which is C. elegans PAMP. At page 34, para. 1 of the instant specification, the specification teaches that this C. *elegans* homologue of PAMP is identical to the sequence

disclosed by the Consortium. Claims 35 and 36 is anticipated by The Consortium because one PAMP can be considered to be a mutant of the PAMP of another species; thus, the C. *elegans* PAMP is a mutant of the human, mouse, and *Drosophila* PAMP, for example. The C. elegans PAMP is considered to be substantially homologous to human, mouse, or D. melanogaster PAMP. Additionally, the C. *elegans* PAMP would be considered to comprise a functional fragment of the human, mouse, and *Drosophila* PAMP, for example.

Applicants urge that the sequence similarity between human and C. elegans PAMP is 22% and therefore C. elegans PAMP is not a function conservative variant of human PAMP. The claims are drawn to homologues, which are not based on sequence identity.

Applicants urge that homologues are those of greater than 80% sequence identity. Homologues are not defined by sequence identity; rather, a homologue is based on qualitative parameters and not quantitative parameters. Further, "substantially homologous" is open to any interpretation.

New Objections and Rejections:

Claim 36 is objected to because of the following informalities: Claim 36 is dependent from non-existent Claim 39. For examination purposes, Claim 36 has been taken to depend from Claim 35. Appropriate correction is required.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 35 and 36 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The mutant PAMP, which is considered to be a

naturally occurring PAMP of a species different from human, mouse, or D. melanogaster PAMP, is not stated to be isolated or purified.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 35-37 are rejected under 35 U.S.C. 102(b) as being anticipated by a single amino acid, such as alanine.

Claims 35 and 37 are drawn to a fragment of mutant PAMP, this fragment having no assigned activity. Therefore, a fragment of mutant PAMP is alanine, for example.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 35-37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The fragment of a mutant PAMP has no defined activity in the claims. Thus, the claims lack written description because there is no correlation of structure and function. Thus, Applicants are not in possession of fragments of mutant PAMP.

Factors to be considered for written description are:

1. level of skill and knowledge in the art: is high.

2. partial structure: The structure of several PAMPS are taught in the specification but that part of the full-length structure that represents a fragment having function is not taught.

3. physical and or chemical properties: The structure of full-length PAMP is known, as are 4 mutations as set forth in Claim 37.

4. functional characteristics alone or coupled with a known or disclosed correlation between structure and function: No characteristics are taught.

5. method of making the claimed invention: One can make fragments of PAMP but one cannot test fragments for unknown activity.

Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to he conclusion that the applicant was in possession of the claimed species of the invention is sufficient (MPEP 2163).

Claim 34 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 34 is drawn to functional conservative fragments of various PAMPs. The term "functional conservative fragments" of PAMP is not taught in the specification. At page 15, paragraph 2, "function-conservative variants" are defined:

"Function-conservative variants" are those in which a given amino acid residue in a protein or enzyme has been changed ***without altering the overall conformation and function of the polypeptide***, including, but not limited to, replacement of an amino acid with one having similar properties (such as, for example, polarity, hydrogen bonding potential, acidic, basic,

hydrophobic, aromatic, and the like). Amino acids with similar properties are well known in the art. For example, arginine, histidine and lysine are hydrophilic-basic amino acids and may be interchangeable. Similarly, isoleucine, a hydrophobic amino acid, may be replaced with leucine, methionine or valine. Such changes are expected to have little or no effect on the apparent molecular weight or isoelectric point of the protein or polypeptide. Amino acids other than those indicated as conserved may differ in a protein or enzyme so that the ***percent protein or amino acid sequence similarity between any two proteins*** of similar function may vary and may be, for example, from 70 % to 99 % as determined according to an alignment scheme such as by the Cluster Method, wherein similarity is based on the MEGALIGN algorithm. A "function-conservative variant" also includes a polypeptide or enzyme which has at least 60 % amino acid identity as determined by BLAST (Altschul SF, *et al.*, J Mol Biol 1990; 215: 403-410) or FASTA algorithms, preferably at least 75 %, most preferably at least 85 %, and even more preferably at least 90 %, and which has the same or substantially similar properties or functions as the native or ***parent protein or enzyme*** to which it is compared.

This definition is silent regarding fragments of PAMP. Therefore, this term found in new Claim 34 is new matter.

At page 6 of their response, Applicant state that no new matter has been added to the specification and point out the definitions at page 15 and now cancelled Claims 1-3. See also page 7 of the response. Canceled claims 1-3 referred to "functional fragments", and page 15 refers to function conserved variants of full-length protein that retain structure (conformation) and function.

No Claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Cochrane Carlson, Ph.D. whose telephone number is 571-272-0946. The examiner can normally be reached on 7:00 AM - 4:00 PM, off alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Kathleen Kerr Bragdon can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Karen Cochrane Carlson PhD

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER